mortality, recruitment was slow and the study was terminated early. The prehospital treatment resulted in an average time savings of 55 min from the time of onset of symptoms to initiation of treatment (130 min for the prehospital group vs. 190 min for the in-hospital group). Total mortality was reduced by 12% (p = 0.08) and cardiac mortality by 16% (p < 0.05) in prehospital-treated versus hospital-treated patients. The greatest effect on mortality was when treatment differences were >90 min between the two strategies.

The Grampian Region Early Anistreplase Trial (GREAT) was a study of 311 patients aimed at evaluating prehospital-initiated fibrinolytic therapy, this time given by general practitioners in patients' homes as compared with after hospital arrival. The average time to treatment was 101 versus 240 min, respectively. At three-month follow-up, patients treated in the prehospital group had fewer Q wave myocardial infarctions and had improved left ventricular function (236). The one-year mortality was substantially lower in the prehospital treatment group (10.4% vs. 21.6%, p = 0.007).

The Myocardial Infarction Triage and Intervention (MITI) trial was the largest randomized prehospital trial in the U.S. It included 360 patients who were initially screened by paramedics utilizing a checklist and ECGs, which were transmitted by cellular telephone to a base station physician for the assignment of treatment. The trial only included patients with a short time to treatment for chest discomfort onset in both prehospital versus hospital initiated thrombolysis groups (92 vs. 120 min, respectively). The prehospital treatment strategy, therefore, provided only a modest time savings of 33 min. There was no significant difference in complication rates between treatment strategies, suggesting that paramedic-administered treatment could be safe. The primary end point of the trial was a ranked composite score that included death, stroke, serious bleeding and infarct size measured by sestamibi imaging. The composite score was similar for both strategies (53% vs. 54%), infarct size (6.1% vs. 6.5%) and mortality (5.7% vs. 8.1%). To further explore the effect of treatment time, a secondary analysis was performed on all randomized patients. There were marked differences in both infarct size and mortality between patients treated within 70 min and those treated between 70 min and 3 h (1.2% vs. 8.7%, p = 0.04).

In a meta-analysis of the three major trials and from five smaller trials, there was a significant reduction in mortality among patients randomized to prehospital therapy (p = 0.002). It was estimated that the benefit–time gradient at 35 days was 21 lives saved per thousand treated per hour (237). These trials have suggested that when long delays of 60 to 90 min or greater are routine, then prehospital initiation of fibrinolytic therapy should be considered. It is clear, however, that prehospital electrocardiography performed by paramedics appears to reduce the total time to treatment and allows for preparation of staff at the receiving hospital. Most data also suggest that the time benefit of treatment is
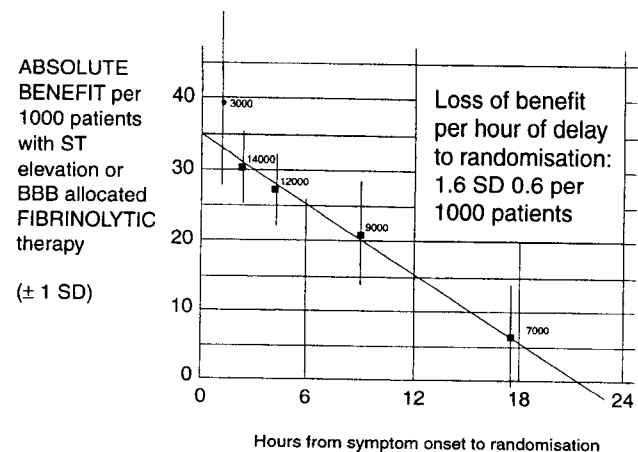

Figure 1. From Fibrinolytic trialists collaboration. Lancet 1994; 343:311–20.

not linear, and that the magnitude is much greater in patients seen in the first hour as compared with 2 to 12 h (238) (Fig. 1). Unfortunately, few patients present to hospital within the first 60 to 90 min, making this strategy less attractive. The current approach requires an extensive expenditure of resources and organization for the benefit of a relatively small fraction of patients. Hospitals have markedly reduced the time to treatment in recent years from hospital arrival to thrombolytic therapy, whereas symptom onset to hospital arrival was unchanged at 2.4 h in the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes trials over a seven-year period (182). Similar observations were made in the National Registry of Myocardial Infarction registry in over 250,000 patients treated with fibrinolytic therapy over a five-year period. Some studies have recently shown that treatment times are now in the neighborhood of 15 to 20 min. Both the EMIP and MITI trials have shown a substantially declining benefit of fibrinolytic therapy as a function of time. They provide community emergency services and hospitals an impetus for improving critical care delivery to patients with AMI.

REGIONAL PLANNING

Regional plans should be established to determine the manner of delivering emergency cardiac services. These plans should integrate the uses of various emergency resources, including both prehospital and hospital resources.

The regional plan should set out the appropriate criteria of how a patient is allocated to a particular hospital. Many systems currently require that the patient be taken to the closest facility. Other systems take the patient to the hospital of the patient's choice, as long as the system has the necessary resources to provide transport to another facility and the patient is stable. These simple policies fail to take into account how they affect the delivery of optimal care to

Table 2. Mortality Rates of Subsets of patients in Randomized Trhombolysis Trials

Variable	FTT	GUSTO-1	GUSTO-3
Age >75 years	25%	21%2	20%
HR >100 beats/min	20%	16%	18%
BP <100 mm HG	28%	16%	18%
Diabetes	14%	11%	12%

BP = blood pressure; FTT = Fibrinolytic Therapy Trialists; GUSTO = Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes; HR = heart rate.

Table 3. Mortality Rates for the Two Forms of Reperfusion as Determined in a Meta-analysis of Randomized Trials (From Primary Coronary Angioplasty Thrombolysis Collaboration)

Variable	Primary PTCA	Thrombolysis
Anterior infarct location	8%	15%
Age >70 years	13%	24%
Previous MI	10%	23%
Diabetes	9%	19%

MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

the cardiac patient. Transport to the closest facility may not be appropriate if the patient has been recently cared for at another facility or is at high risk of complications after myocardial infarction. In contrast, the closer facility may be able to provide care more quickly. Hospital crowding and bed availability should also be considered in the plan. These competing concepts must be considered in the planning process. A triage plan is particularly important for patients at high risk of death.

The hospital facilities in many urban and suburban areas vary widely, with some providing 24 h full tertiary cardiac services, others having inconsistent staffing with a catheterization laboratory but no surgery on site and still others having no tertiary cardiac services. Coronary care units, on the other hand, are common in all areas. The logical question, therefore, is should patients with AMI be diverted to places with full tertiary cardiac services? Unfortunately, this question has not been studied directly in any great detail. Throughout the U.S., patients with trauma are diverted depending on the severity of the illness and resources of the recovery hospital. This severity is gauged through assessment of various factors associated with type of injury as well as the initial clinical findings. Previous studies of elderly (Medicare) patients have suggested that the initial early treatment of AMI within the first day was the major determinant of survival at four years. In addition, this study showed that patients who lived within 2.5 miles of a hospital with cardiac catheterization facilities were substantially more likely to be admitted to a high volume AMI hospital (67% vs. 37%) and to undergo cardiac catheterization within seven days (21% vs. 11%), with a 1% absolute lower rate mortality at one year, as compared with patients living >2.5 miles away (239). These findings have been strengthened by the observations that patients admitted to a high volume hospital (>1.4 AMIs per week) had a lower mortality at one year (27% vs. 30%) than those admitted to a lower volume hospital (<1.4 AMIs per week). These findings were consistent across a variety of high and low risk criteria, but were not associated with a greater use of revascularization (240). However, the link between outcomes after AMI may be closely related to the more appropriate use of "evidence-based medicine" rather than the technology used (241).

Large, randomized trials of thrombolytic therapy have shown that the 30-day and one-year mortality rates are closely related to certain baseline characteristics such as age, blood pressure, heart rate and signs of heart failure (167). The overall 30-day mortality rate from a variety of trials has been between 5% and 10%, whereas in certain subgroups the mortality has been substantially higher (Table 2) (242–244).

For patients with cardiogenic shock, the mortality has remained >50% in the majority of studies and has not changed over time (245). The same risk factors described earlier are also predictive for the development of cardiogenic shock, which typically occurs within the first 6 to 12 h after arrival to the hospital. These findings suggest that certain patient groups with heightened risk can be easily identified by simple measures.

Although individual randomized trials of thrombolysis versus primary PTCA have been done, a meta-analysis of the available data suggests that primary PTCA may be most advantageous among high risk patients (as defined earlier). The outcomes comparing one-year mortality from the meta-analysis (246) suggest particular benefit with primary PTCA among the high risk patients (Table 3).

Patients with cardiogenic shock represent the highest risk group. A prospective, randomized trial has identified a trend toward a reduction in 30-day mortality in patients randomized to emergency revascularization within 6 h of onset of shock as compared with a conservative approach (247). The benefit was seen across all groups, but was particularly apparent in patients <75 years old (41% vs. 57%). On the basis of these observations, it would appear that high risk patients with AMI should be triaged to a high volume AMI center that routinely (24 h service) offers emergency revascularization (PTCA and CABG) if the facility has a transport time of ≤30 min.

CONCLUSIONS AND RECOMMENDATIONS FOR PATIENTS WITH ACUTE CORONARY SYNDROMES

1. Public and professional education should be implemented to increase early recognition of symptoms,

reduce patient delay and enhance appropriate use of EMS systems.

2. The physician should ensure that those patients at risk for an acute coronary syndrome know when and how to react to their symptoms. Risk factor modification should be achieved for all patients.

3. When there is an emergency such as cardiac arrest, chest discomfort or other signs of acute coronary syndromes, 911 should be called directly and should be nationally available as the only emergency call number.

4. The 911 and EMS calls through cellular or digital telephones should have priority over nonemergent calls.

5. All types of telephones should have location identification that is transmitted to the 911 center.

6. All EMS dispatchers should be trained in medical dispatching, including prehospital instructions.

7. Communities should develop plans to optimize triage and treatment of patients with acute coronary syndromes.

8. The EMS providers should use a prehospital chest discomfort checklist.

9. Prehospital 12-lead ECG programs should be imple-mented in established urban and suburban paramedic systems.

10. Prehospital 12-lead ECG programs should communi-cate the prehospital findings to the receiving emergency physician before patient arrival.

11. Prehospital 12-lead computer-interpreted ECGs and predictive instruments should be prospectively validated.

12. Patients with myocardial infarction and hemodynamic compromise, cardiogenic shock or other high risk criteria should be triaged to medical facilities that have 24 h staffed cardiac care services that include emergency revascularization (percutaneous coronary intervention and CABG) and hemodynamic support available, pro-vided ambulance transport duration is not excessive (>30 min). Triage should be performed as soon as possible, preferably in the field or in the nearest Emergency Department, depending on the medical community.

13. Routine prehospital thrombolytic therapy is currently not warranted, except possibly in systems with long transport delays and experienced EMS teams.

Task Force 2: Acute Coronary Syndromes: Section 2B—Chest Discomfort Evaluation in the Hospital

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RATIONALE

Reliable, cost-effective management of patients presenting to the Emergency Department (ED) with chest pain re-mains a major clinical challenge. There are over five million annual visits to EDs in the U.S. for this problem, resulting in two million hospital admissions at a cost of $8 billion (248), and three-fourths of these admissions for presumed myocardial ischemia or infarction prove to be incorrect (249). The primary goal in the management of patients presenting with chest pain is rapid recognition and man-agement of a cardiac ischemic event. Secondary goals include assessment of risk in patients with suspected isch-emia and minimization of unnecessary admissions for low risk conditions. Because of the focus on patient welfare and the litigation potential for failure to detect myocardial infarction (MI), a low threshold for admission has been applied in these patients, but 2% of patients with MI are discharged inadvertently, and the morbidity and mortality of this group are substantial (250). Underscoring this problem are data indicating that failure to diagnose MI has been the leading cause of medical malpractice awards against ED physicians (251).

Nontraumatic chest discomfort remains the primary stimulus triggering evaluation of patients for possible acute coronary syndrome (ACS) in the ED. The ACSs include unstable angina, non–Q wave MI and Q wave MI. To be included in the American College of Cardiology registry for ACS, ST segment changes must be present. However, for this report, ACS includes those patients with suggestive clinical presentations and/or positive biomarkers with or without ST segment changes (252). The clinician in the emergency setting must be suspicious, however, of atypical presentations for ACS. It is essential that emergency phy-sicians be able to make a rapid, carefully focused clinical assessment to identify patients with ST segment elevation MI. Of patients presenting to the ED with chest pain, ~95% do not have electrocardiographic (ECG) evidence of evolving Q wave MI, and only 20% will ultimately have

evidence of unstable angina or non–Q wave MI (249). After the initial evaluation, including a directed history, physical examination and 12-lead electrocardiogram other methods must be used by the clinician to detect ACS in the ED. If the 12-lead ECG is nondiagnostic for ST segment elevation acute MI, patients with a possible ACS must be evaluated for 1) myocardial necrosis; 2) rest ischemia; or 3) exercise-induced ischemia (253). Many hospitals have developed a protocol-driven approach to achieve these objectives (254,255). Through efficient evaluations that take 6 to 12 h, myocardial necrosis is detected by cardiac biomarkers; rest ischemia is documented by serial ECG or ST segment trend monitoring and, if needed, echocardiographic or radionuclide studies; and exercise-induced ischemia is assessed by exercise testing, stress echocardiography or radionuclide testing.

A comprehensive, protocol-driven approach is essential because it minimizes variability in diagnosis and treatment of ACS and promotes optimal management. The evaluation must be complemented by careful documentation of diagnostic results and treatment. Communication with the patient's primary physician is essential to ensure appropriate evaluation and treatment in the ED, and care must also be coordinated with the cardiovascular specialist, when appropriate.

Evaluation in the hospital ED or chest pain center (CPC). Chest pain centers or programs were initially developed to facilitate therapy for patients with acute MI and other ACSs (253,256–259). Their number has grown continuously, and they have subsequently evolved to include safe, cost-effective management of low risk patients presenting with chest pain. It was recently estimated that 30% of hospitals in the U.S. have these units, which number ~1,200 (256).

The rapid increase in CPCs was stimulated in the early 1980s by the need to reduce time to coronary reperfusion therapy (257). The necessity for safer, more cost-effective management of low risk patients, who comprise the majority presenting to the ED with chest pain, has been a major factor in their continuing growth (206,260–262).

Chest pain units vary in form and may be based more on process and coordination of skilled personnel (cardiologists, emergency physicians and nurse specialists) and availability of dedicated equipment than on physical structure. Emphasis is on protocol-based, systematic management to promote optimal application of current standards of care. Guidelines, or critical care pathways, are commonly employed. There are few controlled trials on the utility of CPCs in the management of high risk patients, but the importance of rapid coronary reperfusion therapy is incontrovertible. Recent data demonstrate the efficacy of achieving this objective with a chest pain unit strategy (263). In addition, the importance of early stratification of patients into high and low risk groups is emphasized in the first published guideline for the management of unstable angina (264).

The emphasis of CPCs is variable. Some focus on high risk patients, whereas others primarily aim to decrease unnecessary admissions of low risk patients. In addition to a directed history, physical examination and administration of aspirin, current recommendations include ECG acquisition and interpretation within 10 min to detect myocardial ischemia and make a decision regarding coronary reperfusion therapy, which should be initiated within 30 min of presentation in appropriate patients (188,265,266). Many clinicians advocate briefer time limits for assessment and initiation of therapy (e.g., <20 min). Patients with non–ST segment elevation ischemic syndromes also require prompt identification and treatment. These two groups of patients are recognized as high risk and are transferred to the inpatient service for further management.

In contrast, low risk patients with chest pain, characterized by a stable clinical status and a normal or nondiagnostic ECG, have been increasingly managed by a variety of accelerated diagnostic protocols, usually 6 to 12 h of monitoring and serial cardiac biomarkers (254). If this evaluation is negative, exercise testing (or another noninvasive cardiac stress study) is usually performed, and the patient is discharged if there are no abnormalities. Multiple techniques are currently being assessed for detection of myocardial ischemia during accelerated diagnostic protocols. These include innovative ECG methods, clinical algorithms, new biomarkers, noninvasive cardiac imaging and immediate exercise testing (255). It has been amply demonstrated that accelerated diagnostic protocols utilizing one or more of these techniques in patients identified as low or intermediate risk on the basis of their initial presentation are safe and accurate. Length of stay has been consistently reduced, and subsequent risk in patients with negative evaluations is low. Initial data suggest this strategy is cost-effective, but controlled studies are few, and it is recognized that this approach has the potential for overutilization of expensive tests.

Link between the "chest pain ED movement" and the chest pain awareness educational program. One goal of the "Chest Pain ED Movement" has been development of a partnership between emergency physicians and cardiologists in a continuous quality-improvement process to enhance delivery of heart attack care through community penetration that links the CPC with an early symptom community awareness program. A major focus of this strategy is addressing reasons for delay when patients are having early symptoms. One focus should be on patients presenting with central chest discomfort, not necessarily perceived as chest pain, as well as those with chest pain. Thus, the CPC movement is a strategy to reduce the time to treatment in patients with evidence of early active ischemic heart disease. The new paradigm, as seen in this light, represents a shift in care to enhance present day management of patients with ischemic heart disease.

Operational plan of the CPC. The development and effective operation of a CPC require coordination at multiple levels within the institution, including 1) administrative support (budget, personnel); 2) development of a protocol by emergency physicians, cardiologists and nurses; and 3) integration of special services such as exercise testing, nuclear cardiology, echocardiography and pharmacy. Of primary importance, optimal management in CPCs is critically dependent on communication between the cardiologists and ED physicians.

STAFF. The location of the CPC typically determines the mix of personnel needed to staff the unit. If it is contiguous with the ED, emergency nurses often staff the program. This requires a nurse to patient ratio of approximately 1:4, similar to that of noncritical care areas of the ED or a coronary care unit (CCU) step-down unit. Special training of emergency nurses is necessary before working in a CPC environment. This may include information regarding biomarkers, serial 12-lead electrocardiography or ST segment trend monitoring, exercise testing, echocardiography and radionuclide testing. The CPC stay is also an excellent opportunity to educate patients about ACS, risk factors and the importance of timely follow-up with a cardiologist or other appropriate physician if the evaluation is negative.

Nurse practitioners and physician assistants may help to staff CPCs, but decisions to treat, admit or release the patient require physician involvement in every step of care and are the responsibility of the attending physician. Technicians who perform studies such as echocardiography or nuclear cardiology are essential and must have the flexibility to follow protocols. The availability of technicians at night or on weekends determines not only the frequency of testing, but also the ability of a CPC to extend service beyond the traditional scheduling limits.

PHYSICIANS. If the CPC is located in or next to the ED, emergency physicians are responsible for evaluating and monitoring patients, administering therapy and developing disposition plans for hospital admission or discharge. The CPC requires 15 to 20 patients at a time to justify the presence of a dedicated emergency physician at all times. Smaller CPCs are usually served by physicians with other responsibilities in the ED. Typically, two or more physicians working simultaneously in the ED are necessary to allow sufficient free time to attend to patients in the CPC.

In CPCs in or next to the ED, emergency physicians monitor symptoms and signs, interpret diagnostic tests and initiate therapy for patients admitted with ACS. As a functional component of an ED, the availability of an emergency physician 24 h per day, seven days per week remains an essential component. Offline discussions regarding protocols with referring physicians, clinical pathologists and cardiologists ensure a consistent approach to evaluation, treatment, patient education and follow-up plans for patients discharged. Such communication with cardiologists allows a coordinated approach to administering antiplatelet and antithrombotic agents, nitroglycerin and beta-blockers in a protocol-driven manner. For patients with ST segment elevation consistent with acute MI, fibrinolytic therapy is usually administered without previous consultation with a cardiologist. In hospitals where primary angioplasty is available, communication with the interventional cardiologist is necessary to decide between thrombolysis and primary angioplasty and to coordinate mobilization of the cardiac catheterization laboratory team if the latter therapy is selected.

In institutions where the CPC is located in the CCU or serves as a part of an inpatient step-down unit, cardiologists (or internists) are responsible for serial examinations, interpretation of diagnostic testing and, if such testing is positive for an ACS, therapeutic directives.

For CPCs adjacent to the ED or CCU, cardiologist involvement in the care of the patient at the end of a 6 to 12 h protocol is often necessary to interpret predischarge tests such as exercise electrocardiography or imaging. The decision to admit a patient to the hospital or discharge the patient often requires the collaboration of the cardiologist and the physician responsible for the patient in the CPC. In institutions without a structurally designated CPC, the goals of this strategy can be implemented by adhering to protocols that focus and coordinate the efforts of the diverse personnel noted earlier to provide optimal management of patients presenting with chest pain. In this approach, the CPC process remains foremost.

INITIAL TRIAGE

The goals of clinical assessment of the patient with chest pain are 1) to distinguish those patients with ischemia or infarction from those with other potentially serious (aortic dissection, pericarditis, pulmonary embolism) or less serious causes of chest pain; 2) to assess the risk of early adverse outcomes in patients with suspected ischemia or infarction; and 3) to initiate therapy rapidly in patients with serious clinical conditions. Initial evaluation of the patient with chest pain includes a careful history and physical examination and, in almost all cases, an ECG. It may be performed by emergency medical service personnel, the triage nurse, physician or other medical personnel. The evaluation may begin at home, at the work site or another location and continue during transfer and in the ED or outpatient facility. Patients with probable ischemic pain and patients with high risk features such as severe or prolonged pain or hemodynamic compromise should be transported to the ED by ambulance. Proper assessment at this point is critical to the efficacy and cost-effectiveness of subsequent testing.

Differential diagnosis of chest pain. Until recently, the description of the characteristic pain of myocardial ischemia was based almost exclusively on data from men. However, a number of patient groups commonly present with "atypical" symptoms. In women, ischemia may be manifested by symptoms such as fatigue, dyspnea or epigastric pain. Other groups commonly presenting with atypical symptoms in-

clude diabetics and the elderly. These factors must be incorporated into the clinical evaluation.

CORONARY ARTERY DISEASE (CAD). The key factors in recognizing ischemia in the ED are the characteristics of the symptoms, the ECG, a history of CAD and evidence of hemodynamic or electrical instability. The presence of coronary risk factors may be a helpful predictor, but is of limited utility and may even be misleading in this setting, as compared with other variables such as the ECG. However, in the absence of strong clinical or ECG evidence of ischemia, assessment of risk factors has value. The discomfort or pain of myocardial ischemia or infarction is generally described as tightness, heaviness, pressure, burning, aching, squeezing, constriction or "indigestion." It usually comes on gradually over a minute or two and lasts minutes rather than seconds. It is usually not affected by respiration or changes in position. It is usually felt in the central chest, with other common sites including the throat, jaw, back, epigastrium, left chest and arm (usually left). Associated symptoms include sweating, dyspnea, nausea, vomiting, lightheadedness, weakness and malaise.

Typical angina is precipitated by physical or emotional stress and is relieved by rest. The discomfort of stable angina (most often *not* described as pain) is often relieved or lessened within 2 to 5 min of the administration of sublingual nitroglycerin. Ischemic pain due to infarction may not be relieved by nitroglycerin. On physical examination, particular attention should be directed to signs of pulmonary congestion and the presence, during symptoms, of an S_3 or paradoxic splitting of S_2 (sign of systolic left ventricular dysfunction), an S_4 (sign of diastolic dysfunction) or a murmur of mitral regurgitation (sign of papillary muscle dysfunction). Peripheral pulse deficits, or bruits, are valuable clues to the presence of atherosclerosis, aortic dissection or, rarely, vasculitis.

Electrocardiographic tracings should be obtained whenever possible in both the presence and absence of chest pain. The ECG should be examined for evidence of a previous MI. ST segment elevation ≥ 1 mm is generally indicative of acute MI, but must be distinguished from other conditions (e.g., early repolarization, pericarditis). Lesser degrees of ST segment elevation are less specific for MI. Any ST segment or T-wave abnormalities that are observed in the presence but not in the absence of chest pain are suggestive of myocardial ischemia. Peaked T-waves may be due to hyperkalemia or may be a hyperacute manifestation of ischemia. Fixed ST segment and T-wave abnormalities are usually less specific, but are suggestive of myocardial ischemia or infarction if there is ≥ 1 mm ST segment depression or elevation or deep symmetrical T-wave inversion. In contrast, a normal ECG does not reliably exclude the diagnosis of myocardial ischemia (or even infarction). It is often helpful, and in some clinical presentations essential, to obtain frequent serial ECGs (266).

PERICARDITIS. Pericarditis may occur in patients with connective tissue disease, malignancy, previous radiation, recent MI or thoracotomy or uremia or in previously healthy individuals. The pain is usually sharp, midcentral in location and worsened by inspiration or lying down. It may be felt in the left chest, supraclavicular area, shoulder and, rarely, the back. Fever may be present; difficulty taking a deep breath should be distinguished from true dyspnea. A two- or three-component pericardial friction rub is pathognomonic of pericarditis. Pulsus paradoxus and jugular venous distention suggest pericardial tamponade. Diffuse ST segment elevation, as well as PR segment depression, strongly supports the diagnosis of acute pericarditis. Further evaluation includes a chest radiograph and echocardiogram.

AORTIC DISSECTION. Patients with hypertension, Marfan's syndrome, trauma or bicuspid aortic valve or previous aortic valve surgery and those who are pregnant are at risk for dissection of the thoracic aorta. The pain of dissection is usually abrupt in onset and is often described as ripping or tearing, but may be similar to the pain of myocardial ischemia. It is located in the chest or back, or both, and may radiate to the teeth. Associated symptoms are related to affected branches of the aorta and include angina, dizziness and other neurologic complaints. Physical examination may reveal unequal arm blood pressures, pulsus paradoxus (due to associated cardiac tamponade), signs of left pleural effusion, aortic insufficiency and pulse deficits. The ECG may reveal myocardial ischemia (usually in the distribution of the right coronary artery). When the initial assessment suggests aortic dissection, imaging with chest radiography, transesophageal echocardiography, computed tomography or magnetic resonance imaging, or a combination of these, is appropriate. Fibrinolytic therapy should not be initiated if the diagnosis of aortic dissection is being considered seriously in the differential diagnosis.

PULMONARY EMBOLISM. Patients at risk for pulmonary embolus include those with pelvic or leg trauma, previous surgery, immobility, obesity and hypercoagulable states. "Pleuritic" chest pain results from pulmonary infarction. Substernal pressure or discomfort may be due to right ventricular ischemia resulting from an increase in pulmonary vascular resistance and a decrease in systemic arterial pressure, and thereby coronary perfusion pressure. Tachypnea and tachycardia are common findings. In the presence of massive pulmonary embolus, the ECG may show an S_1-Q_3 pattern, a rightward axis and right precordial T-wave inversions. Further evaluation may include a $\dot{V}Q$ scanning, contrast spiral computed tomographic scanning, pulmonary angiography and noninvasive evaluation of leg veins. Unless there is a contraindication, heparin is begun when the diagnosis is first discussed.

OTHER CAUSES OF CHEST PAIN. Exertional (and, rarely, rest) angina can occur in patients with aortic stenosis,

hypertrophic cardiomyopathy, pulmonary hypertension or pulmonic stenosis. Chest pain may be caused by a thoracic aortic aneurysm, pleuritis and pneumothorax. Of several gastrointestinal causes of chest pain, esophageal spasm is noteworthy in that it may be relieved by nitroglycerin. The pain of herpes zoster may bring patients to medical attention before bullae appear. Various musculoskeletal disorders, including arthritis of the cervical spine, costochondritis and chest wall muscle injuries may cause pain that mimics angina. Careful palpation of the chest wall may indicate point tenderness and reproduce the patient's presenting symptom.

LOW RISK PATIENTS

The low risk population can be readily recognized in most cases from the initial clinical presentation and the ECG. Patients with chest pain with a risk of MI <5% and a risk of cardiac complications <1% can be identified by this approach (267). Patients with negative findings after evaluation in the CPC of the ED usually have noncardiac etiologies of their symptoms and often require further outpatient studies to determine the cause of their symptoms so that appropriate therapy can be initiated. It is essential that further evaluation be done in conjunction with the patient's primary physician. Noncardiac conditions (e.g., gastrointestinal, musculoskeletal, pulmonary, psychological) may be responsible for chest pain symptoms that initiate a cardiac evaluation. Too often, evaluation ends with the negative cardiac workup. Identification of the etiology of symptoms in this sizable group of patients has the potential to ameliorate the patient's problem and avoid unnecessary return to the ED. In some patients, even the most thorough evaluation for noncardiac sources of pain is unrevealing. These patients rarely have a life-threatening problem, but their symptoms may be disabling. A physician expert in pain management may be helpful in such cases. Up to 40% of patients with a negative workup have chest pain related to panic attacks. This is infrequently recognized by physicians during the acute episode and on follow-up (268). Somatization syndrome (multiple symptoms across organ systems without an organic basis) is a relatively common noncardiac cause of chest pain in patients presenting to the ED. If patients meet the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) (269) criteria for diagnosis, consideration of cardiac disease should be based on objective findings. Other patients with nonischemic pain may have what has recently been termed the "sensitive heart," in which normal physiologic stimuli (e.g., changes in intracardiac pressure, blood flow and heart rate) are sensed as discomfort or pain in the chest (270). In contrast, some patients with chest pain have myocardial ischemia with angiographically normal coronary arteries (syndrome X) (271).

ASSESSING LEVELS OF RISK AND APPROPRIATE INITIAL MANAGEMENT IN PATIENTS WITH MYOCARDIAL ISCHEMIA OR INFARCTION (HIGH RISK PATIENTS)

Once the diagnosis of myocardial ischemia or infarction is made, the clinician must assess the history, physical examination and ECG to determine 1) the pace of initial therapy, including acute reperfusion strategies, if indicated (266,272); and 2) the appropriate next step in evaluation if reperfusion therapy is not indicated.

Appropriate patients with ST segment elevation MI should receive coronary reperfusion therapy. Selected high risk individuals with non–ST segment elevation ACS should be admitted for intensive medical management or coronary angiography (264,266,272).

INTERMEDIATE RISK PATIENTS: FURTHER EVALUATION

Continuous ST segment ECG monitoring and non-standard ECG lead systems: use in patients with chest pain who present to the ED. The rest 12-lead ECG is the standard of care in the diagnosis of patients with chest pain seen in the ED. Approximately 50% or less of patients with acute MI or ACS initially have a positive 12-lead ECG. Because early diagnosis is crucial to myocardial salvage, newer strategies have been advocated for increasing the sensitivity of the 12-lead ECG. These include serial electrocardiography, continuous ST segment ECG monitoring and the use of nonstandard lead systems, including posterior and right ventricular leads. Recommendations for the use of newer diagnostic technologies should rely on prospective, randomized studies that 1) clearly show an incremental benefit in terms of either diagnosis or prognosis; 2) take into account the availability, ease of use and applicability; and 3) demonstrate cost-effectiveness. Sensitivity and specificity are important measures of a diagnostic test, but positive and negative predictive values, which are highly dependent on the prevalence of disease in the population tested, are more important in determining the incremental value of a new test or procedure.

STANDARD ECG. A 12-lead ECG should be obtained on admission and repeated in 15 to 30 min if there is high suspicion of myocardial ischemia or if there is recurrent chest pain. In patients with negative accelerated diagnostic protocols, a repeat ECG should always be obtained before stress testing.

CONTINUOUS ST SEGMENT MONITORING. This technique for detecting ischemia has been studied predominantly in patients with established CAD. Its role in the detection of myocardial ischemia in patients who present to the ED is unclear. In one recent study in a CCU setting (with a high prevalence of CAD), there was a 40% false positive rate of ST segment shift. With the lower prevalence of CAD in

most patients with chest pain who present to the ED, this high incidence of false positive tests would be expected to reduce the positive predictive value of this method. In another study, the sensitivity for detecting acute MI and ACS was increased from 55.4% to 68.1% using continuous ST segment monitoring as compared with the initial ECG, with a corresponding increase in the likelihood ratio of 10.3 to 13.1. In one additional study performed in a CPC/ED protocol, the sensitivity of serial ST segment monitoring was 21.2%, and the positive predictive value was 64.7%. However, its additive value was unclear. In summary, the cost-effectiveness of ST segment monitoring used in concert with other measures has not been assessed directly, and thus its role in the ED for patients with chest pain is uncertain.

RIGHT-SIDED ECG LEADS. The sensitivity of the standard 12-lead ECG in diagnosing right ventricular and posterior infarction is extremely low. These limitations have given rise to the evaluation of a number of nonstandard lead placement systems. The most common of these are right ventricular leads, of which the most sensitive is V_4R. The sensitivity and specificity for diagnosis of right ventricular infarction with the V_4R lead is ~80% during the initial 24 h of infarction. A number of prospective studies have demonstrated that right ventricular MI is a significant negative prognostic factor in patients with coexistent inferior wall MI. A V_4R lead should be recorded at least once, as early as possible, in all patients with inferior or inferoposterior wall MI.

POSTERIOR LEADS. The 12-lead ECG is least sensitive for detection of posterior ischemia in the distribution of the left circumflex coronary artery (273). The use of leads V_7 through V_9 offers incremental benefit for diagnosing posterior MI. The use of posterior ECGs leads V_7 through V_9 is appropriate if there is suspicion of posterior infarction. It cannot be recommended routinely for all patients presenting to the ED with chest pain.

Biomarkers of cardiac injury for the treatment of low risk patients. Two strategies have competed in this area. The first relies on two markers—a rapid rising marker and a marker that takes longer to rise but is more specific. This strategy is predicated on the assumption that early diagnosis of MI will change care by:

1. Facilitating identification of patients who may be candidates for aggressive intervention.
2. Streamlining and improving flow within the CPC/ED setting.
3. Providing the ability to discharge patients earlier.
4. Facilitating the triage of patients who are admitted to various parts of the hospital.

Both myoglobin and isoforms of creatine kinase, MB fraction (CK-MB) have been proposed for this purpose. In the latest trial to date, no statistically significant differences were observed between these markers (274). Myoglobin is rapidly released from the myocardium and therefore is often elevated in the first sample after presentation. Definitive inclusion of infarction takes at least 6 h (274). The failure of myoglobin to change over time by some predetermined amount effectively excludes evolving infarction (275).

Isoforms of creatine kinase function on a different principle. Low levels are present in the blood normally. Thus, sensitive detection of a change can achieve earlier diagnosis.

This strategy allows the early identification of patients without infarction who may need stress testing or other follow-up evaluation. Individuals in whom biomarker levels are increasing require additional sampling for either CK-MB or troponin so that a definitive diagnosis of infarction can be made with markers that have a higher degree of specificity. Both myoglobin and CK-MB isoforms lack tissue specificity. Thus, subsequent samples to diagnose infarction may be needed at 6 and often 9 to 12 h. These samples also allow detection of a subset of patients who may have small amounts of necrosis as documented by a sensitive marker like troponin. This group may have had cardiac insults in the days before admission or a minimal amount of myocardial necrosis more sensitively detected by troponin. Regardless of the mechanism, this group is known to have an adverse short- and long-term prognosis (276–279), and preliminary data suggest that these patients may benefit from more intense therapy (280). Although CK-MB is frequently used at present for definitive "late diagnosis," eventually the troponin markers will replace CK-MB for this purpose.

The troponins (cardiac troponins I and T) are a new class of markers that have unique cardiac specificity (281). It is now clear that for both markers, elevations are indicative of cardiac injury only. In addition, at the present levels of assay sensitivity, the troponins are more sensitive than CK-MB for minor myocardial necrosis (282). Furthermore, continuing release of troponin occurs for many days or even weeks after cardiac injury (283). Inpatients who are at high risk for ischemic heart disease (e.g., patients with unstable angina, elevations) almost always have ischemic injury, and multiple studies have confirmed that elevations presage an adverse short- and long-term prognosis (276–279). Elevations are more problematic in low risk patients. Hamm et al. (284) have shown that elevations identified all of the patients at risk in a cohort of 733 patients with chest pain and nondiagnostic ECGs. Other investigators have shown a significant relation between positive troponins and underlying, severe CAD in otherwise low risk patients in the CPC (285). Elevation of troponins may also occur in a second group of patients who have nonischemic cardiac injury related to a transitory or chronic process. Thus, elevations in low risk patients would not always be associated with CAD.

The second strategy suggests that the urgency is less critical than suggested by the first strategy (286). The tactic involved is simply to measure a single CK-MB or cardiac troponin, with the understanding that definitive exclusion

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or inclusion of infarction will take longer. At present, for the troponins, it appears that at least 9 h is required, depending on the cutoff value utilized, and for CK-MB, the general time is 12 h. These times can be altered somewhat by choosing different critical values for diagnosis. The logic of this strategy insists that marker proteins will not facilitate the evaluation of patients in need of an immediate intervention, because most of these patients present with clinical syndromes and ECG changes that are easily identified. It further argues that discharge and in-hospital triage will not suffer substantially from a 2 to 3 h delay. The advantage of this strategy is that it is definitive in both directions (to include and exclude infarction).

The strategy suggested by Hamm et al. (284) is to use a low cutoff value with troponin markers in serial samples obtained on admission and at least ≥6 h after the onset of symptoms. A low cutoff value uses the level of detectability of the assays, and with that criterion, all patients at risk for events during the first 30 days, even without additional stress testing, are identified. The benefit of this strategy is that it combines the early negative predictive value of rapidly appearing markers with a high level of positive predictive value. The disadvantage of this strategy is that minor elevations of troponin are frequent in patients who have hypertension, congestive heart failure and other clinical syndromes that may cause minimal amounts of myocardial damage.

The rapid availability of test results is essential. Most laboratories acknowledge that a turnaround time of 30 to 60 min for these tests is standard. If the availability of results takes substantially longer, point of care testing should be considered (287). At present, the devices available are not as accurate or as easy to use and interpret as they will likely become; they are also several fold more costly, and regulatory issues add to the difficulty of their use. Nonetheless, their use is advocated if laboratory turnaround times are inadequate for the needs of the patients. It is clear that strategies will need to be developed to accommodate local needs. No matter what strategy is employed initially, it is likely that in the long term, it will evolve into one predicated on troponin markers.

Predictive instruments. The major reasons for development of these decision aids are to standardize care and improve efficiency. Physicians, in general, tend to be risk adverse by nature, overestimate the probability of complications and have a low threshold for admitting low risk patients (288). Accurate estimates of patients' probabilities for complications might support physicians in their transfer of low risk patients to be treated at non-CCU facilities or at home. It has been shown, in patients presenting with chest pain, that ECG and other clinical data predict risk of acute MI (289), and these factors also predict which patients will have complications (267). On the basis of clinical features, patients can be stratified into four groups, with the risk of major complications in the first 72 h ranging from 0.7% to

20% (267). These data can also be used to stratify patients according to their risk of long-term complications (248). Decision aids have been adapted and incorporated into computerized ECG reports to help clinicians in the triage process (234,290).

Although studies continue to show that algorithms based on multivariate statistical techniques have the *potential* to improve medical decision-making (291), prospective trials have consistently shown minimal or no impact of attempts to use these algorithms in practice (292–294). Some data indicate that physicians do not use these algorithms because they are too busy or do not perceive their value (292), or because they are concerned about the medicolegal and clinical consequences of inappropriate discharges of patients (295,296). An important current focus of research is to integrate decision aids into routine data acquisition, such as through predictive instruments (234) or critical pathways (297).

Guidelines and critical pathways. Standards of care for the initial evaluation of patients with chest pain have been developed by several organizations, including the American College of Emergency Physicians (ACEP) (298). These guidelines stress that the decision to admit the patient must be primarily based on clinical judgment and do not make recommendations about levels of care (CCU versus intermediate care of CPC) for different patient subsets. The ACEP statement provides "rules" and "guidelines" about the data that should be obtained, and recorded, as part of the evaluation, as well as the actions that should follow from certain findings. "Rules" are considered actions that reflect principles of good practice in most situations. "Guidelines" in the ACEP document are actions that should be considered; there is no implication that failure to follow a "guideline" constitutes improper care. These guidelines also emphasize the need for a functional design of the program, appropriate staffing, quality assurance and outreach, in addition to the ability to diagnose and initiate therapy in patients with acute MI and unstable angina and to evaluate those low risk patients with chest pain.

The National Heart Attack Alert Program (NHAAP) has issued guidelines for specific functions related to evaluation and treatment of patients with chest pain aimed at improving the speed with which patients with acute MI are identified and treated (265). Guidelines for the care of acute MI and unstable angina are available to direct care for patients with clear evidence of those syndromes (266,272,299).

Guidelines from the Agency for Health Care Policy and Research (AHCPR) for unstable angina indicate that not all patients with this syndrome require admission, but recommend ECG monitoring patients with unstable angina during their evaluation; those with ongoing rest pain should be placed in bed rest during the initial phase of stabilization (264). The ACEP policy statement indicates that patients who are discharged should be provided a referral for

follow-up care, as well as instructions regarding the treatment and circumstances that require a return to the ED (298).

Institutional guidelines to increase efficiency have generally emphasized two strategies: 1) triage of low risk patients to non-CCU–monitored facilities such as intermediate care units or CPCs; and 2) shortened lengths of stay in the CCU and hospital. Recommendations regarding the minimal length of stay in a monitored bed for a patient who has no further symptoms have been decreasing over the last two decades from 24 h (300) to 12 h (301), to even shorter periods if exercise testing or other risk stratification technologies are available (254,297).

Several studies have shown inconsistent application and impact of guidelines. In one study, there was no effect on admission rates, triage decisions or length of stay (293). In another, a 26% reduction in length of stay resulted in use of the guideline (302).

One strategy for optimizing and streamlining care is through critical pathways (297,303). These predefined protocols outline and manage the crucial steps in defining a clinical problem and treating that patient and aim to improve quality of patient care, reduce variability and enhance efficiency. Data are collected to define the rate-limiting steps for each patient group and to provide feedback to health care providers and managers regarding the care rendered.

There are at least two important differences between a critical pathway and more traditional guidelines: 1) critical pathways define time goals for the performance of key tasks; 2) critical pathways should be used to collect information on rates at which these tasks are performed within the target period.

Data on the impact of critical pathways on efficiency and patient outcomes are not yet available. Such data are likely to have limited generalizability, because the effectiveness of a pathway depends heavily on the capacities of the institution in which it is implemented and whether data are fed back to clinicians as part of a quality-improvement process. Furthermore, pathways evolve quickly with the adoption of new technologies such as cardiac markers of injury.

Exercise testing. Recent studies have confirmed the safety, accuracy and utility of early treadmill exercise testing in low risk patients presenting to the ED with chest pain. These data stem primarily from investigations of patients with negative evaluations in accelerated diagnostic protocols (6 to 12 h of monitoring, negative serial cardiac biomarkers) who then undergo predischarge exercise testing. In this context, the test is used to determine the need for further inpatient evaluation (positive test) or suitability for discharge with follow-up (negative test). Accelerated diagnostic protocols, including exercise testing as a key element, have been associated with reduced hospital stay and lower costs. There have been no adverse effects of exercise testing in this setting, and a negative test has accurately identified low

prognostic risk (i.e., patients with negative evaluations on accelerated protocols have had the same posthospital course as those with negative findings with traditional, longer hospital stays) (254,255). Exercise treadmill testing has been adequate for evaluation after a negative accelerated protocol. There are no data indicating that stress imaging tests add to predictive accuracy in this group.

One group has employed "immediate" exercise testing of low risk patients in the ED without previous evaluation by serial cardiac biomarkers (304,305). These patients were clinically stable and had normal or near normal ECGs and a negative screening evaluation (physical examination, chest radiograph). This method has been safe and effective, with no adverse effects of exercise testing in >1,000 patients (306), and has been used to identify patients who could be discharged directly from the ED and those who required admission. However, it has been associated with a low (<1%) rate of inadvertent testing of patients with inapparent non–Q wave MI (306). This approach requires further study.

Echocardiography. Left ventricular wall motion abnormalities in a patient with acute chest pain should be considered suggestive of ischemia (307). However, echocardiography cannot distinguish new abnormalities of wall motion or systolic wall thickening (due to either reversible ischemia or acute infarction) from those that are old (previous infarction), and it may detect abnormalities that are unrelated to ischemia in patients with conduction abnormalities such as paced rhythms and bundle branch blocks, thus limiting its specificity. In addition, with minimal or nontransmural myocardial involvement, even with acute MI, wall motion abnormalities may not be detected by early echocardiography (308).

In general, the sensitivity and specificity of the echocardiogram for detecting acute ischemia as the etiology of chest pain symptoms are best when it is used during or soon after an episode of pain. Small studies in highly selected groups without a previous infarction or other cardiac abnormalities have shown sensitivities and specificities of 86% to 92% and 53% to 90%, respectively, in this setting (207). In one unselected group with chest pain, 94% of patients had technically adequate images for assessment of ischemia, and even in these patients, the sensitivity and specificity were only 93% and 57%, respectively (309). However, echocardiography may provide information such as abnormalities of global left ventricular function or wall motion suggestive of previously unrecognized CAD. Localized wall motion abnormalities may also help identify the culprit artery in acute ischemia.

To be most useful for diagnosis and early risk stratification, the echocardiogram would need to be available immediately in the ED, with highly trained personnel to obtain and interpret the study (310,311). Ideally this service would be immediately available 24 h a day, seven days a week.